

wherein the number of nucleotides between the gene segments within the transgene that encode said mu and said human gamma isotypes is less than the number of nucleotides between the gene segments encoding human mu and said human gamma isotype in the human germline; and

collecting heterologous human gamma immunoglobulins which bind to said pre-selected antigen.

#### REMARKS

Applicants have cancelled claims 1-44 and added claim 45. Claim 45 is the only claim now pending in the application. Support for claim 45 is discussed, *infra*, at pages 5-13.

Claim 45 is copied exactly from claim 1 of United States patent 5,545,806 of Lonberg et al., issued August 13, 1996 ("the '806 patent") (copy enclosed as Exhibit A). Claim 1 of the '806 patent recites:

1. A method for producing heterologous immunoglobulins from a transgenic mouse, the method comprising:

contacting said transgenic mouse with a pre-selected antigen, said transgenic mouse having a genome comprising germline copies of at least one transgene having human sequences  $V_H$  segment genes, human D segment genes, and human  $J_H$  segment genes, wherein the transgene undergoes isotype switching from a transgene-encoded mu isotype to a transgene-encoded downstream human gamma isotype *in vivo*, wherein the number of nucleotides between the gene segments within the transgene that encode said mu and said human gamma